

PATENT CLAIMS

1. A modified molecule having the biological activity of byrodin 1 and being substantially non-immunogenic or less immunogenic than any non-modified molecule having the same biological activity in an individual when used *in vivo*, wherein the said loss of immunogenicity is achieved by removing one or more T-cell epitopes derived from the originally non-modified molecule and said T-cell epitopes are MHC class II ligands or peptide sequences which show the ability to stimulate or bind T-cells via presentation on class II.
2. A byrodin 1 molecule of claim 1, wherein the removing of said T-cell epitopes are achieved by replacing 1 – 9 amino acid residues.
3. A byrodin 1 molecule of claim 1 or 2, wherein said T-cell epitopes are peptide sequences selected from the group as depicted in FIGURE 1.
4. A byrodin 1 molecule of claim 1 or 2, wherein said T-cell epitopes are located within the strings of contiguous amino acid residues termed as R1 – R5 encompassing residues 46-66; 88-102; 112-135; 136-162 and 178-204 of the wild-type byrodin 1 sequence.
5. A byrodin 1 molecule of claim 4, wherein said strings have the following sequences:
 - (a) ITTLYYYTASSAASALLVLIQSTAESA (R1),
 - (b) ATEAAKFVFKDAKKK (R2),
 - (c) ERLQTAAGKIRENIPLGLPALDSA (R3),
 - (d) ITTLYYYTASSAASALLVLIQSTAESA (R4),
 - (e) ATISLENNWSALS KQIQIAST (R5)
6. A byrodin 1 molecule of claim 5, wherein the replacement of amino acid residues is achieved within a sub-string of at least 9 consecutive residues from any of the strings R1 – R5.

7. A byrodin 1 molecule according to claims 4 – 6 sharing amino acid identity with any of the peptide sequence strings R1 – R5 greater than 80%.
8. A byrodin 1 molecule of claim 7 sharing amino acid identity with any of the peptide sequence strings R1 – R5 greater than 90%.
9. A byrodin 1 molecule according to any of the claims 1 – 8, comprising the following sequence:

DVSFRLSGATTTTSYGVIKLNREALPYERKVYNIPLLRSSISGSGRYX¹X²LX³LTX⁴X⁵AD
 ETX⁶SVAX⁷DX⁸TNVYIMGYLAGDVSYFFNEASATEAAKX⁹X¹⁰FKDAKKX¹¹TLPYSGNVE
 RX¹²QTX¹³AX¹⁴X¹⁵X¹⁶X¹⁷ENX¹⁸PLGX¹⁹PAX²⁰DSAX²¹TTX²²YX²³X²⁴TASSAASAX²⁵X²⁶X²⁷X²⁸IQSTAESARYKFIEQQIGKRVDKTFPLSLATX²⁹SX³⁰ENNWSAX³¹SX³²QX³³QX³⁴AS
 TNNGQFESPVVLIDGNNQRVSITNASARVVTSNIALLLNRNNIAAIGEDISMTLIGFEHG
 LYGI

wherein

X¹ is A, G or P; X² is M, A, G, P or I; X³ is A, G or P; X⁴ is P or Y;
 X⁵ is T or S; X⁶ is P; X⁷ is A, P or G; X⁸ is A, P or G;
 X⁹ is A, P, G, H, D, E, N, Q, K, R, S or T; X¹⁰ is A, P or G; X¹¹ is A, P or G;
 X¹² is A, P, S, T, H or K; X¹³ is T; X¹⁴ is H; X¹⁵ is S;
 X¹⁶ is A, S, T, P, N, D, E, G, H, K or Q; X¹⁷ is T; or P;
 X¹⁹ is A, I, F, G, M, P, V, W or Y; X²⁰ is F, P or W; X²¹ is A, P or G;
 X²² is G, A or P; X²³ is G, A or P; X²⁴ is A, P or G; X²⁵ is A, P, G, S or T;
 X²⁶ is A, I, M, S, T, P or G; X²⁷ is A, G or P;
 X²⁸ is S, A, G, P, T, H, D, N, Q, K or R;
 X²⁹ is T, A, G, S, P, H, K, R, D, E, N or Q;
 X³⁰ is A, G, S, T, P, K, R, H, D, E, N or Q; X³¹ is Q;
 X³² is H, D, E, F, L, N, P, S, W or Y;
 X³³ is T, A, G, P, D, E, H, K, R, N, Q, S or T; and X³⁴ is D,

and whereby simultaneously

X¹ = T, X² = L, X³ = H, X⁴ = N, X⁵ = Y, X⁶ = I, X⁷ = V, X⁸ = V, X⁹ = F, X¹⁰ = V,
 X¹¹ = V, X¹² = L, X¹³ = A, X¹⁴ = G, X¹⁵ = K, X¹⁶ = I, X¹⁷ = R, X¹⁸ = I, X¹⁹ = L, X²⁰ = L,
 X²¹ = I, X²² = L, X²³ = Y, X²⁴ = Y, X²⁵ = L, X²⁶ = L, X²⁷ = V, X²⁸ = L, X²⁹ = I, X³⁰ = L,
 X³¹ = L, X³² = K, X³³ = I and X³⁴ = I

are excluded.

10. A byrodin 1 molecule of claim 9, wherein X¹ is A, X² is M, X³ is A, X⁴ is P, X⁵ is T, X⁶ is P, X⁷ is A, X⁸ is A, X⁹ is A, X¹⁰ is A, X¹¹ is A, X¹² is A, X¹³ is T, X¹⁴ is H, X¹⁵ is S, X¹⁶ is A, X¹⁷ is T, X¹⁸ is A, X¹⁹ is A, X²⁰ is F, X²¹ is A, X²² is G, X²³ is G, X²⁴ is A, X²⁵ is A, X²⁶ is A, X²⁷ is A, X²⁸ is S, X²⁹ is T, X³⁰ is A, X³¹ is Q, X³² is H, X³³ is T and X³⁴ is D.
11. A modified byrodin 1 molecule according to any of the claims 1 – 10, wherein said molecule, when tested as a whole protein in a biological assay of induced cellular proliferation of human T-cells, exhibits a stimulation index (SI) smaller than the parental non-modified molecule and smaller than 2, tested in parallel using cells from the same donor wherein said index is taken as the value of cellular proliferation scored following stimulation by the protein and divided by the value of cellular proliferation scored in control cells not in receipt of protein and wherein cellular proliferation is measured by any suitable means.
12. A pharmaceutical composition comprising a modified byrodin 1 molecule according to any of the claims 1 – 11 optionally together with a pharmaceutically acceptable carrier, diluent or excipient.
13. A DNA molecule coding for any of the modified byrodin 1 molecules as specified in any of the claims 1 – 12.
14. A peptide being part of the wild-type byrodin 1 and comprising one or more T-cell epitopes being MHC class II ligands or peptide sequences which show the ability to stimulate or bind T-cells via presentation on class II; the peptide is selected from the group:
- (a) RYTLHL¹TNYADETISVAVDV (R1),
 - (b) ATEAAKFVFKDAKKK (R2),
 - (c) ERLQTAAGKIRENIPLGLPALDSA (R3),
 - (d) ITTLYYYTASSAASALLVLIQSTAESA (R4),
 - (e) ATISLENNWSALS¹KQIQIAST (R5).

15. A peptide of claim 14 having a stimulation index (SI) of > 1.8 in a biological assay of cellular proliferation of human T-cells, wherein said index is taken as the value of cellular proliferation scored following stimulation by a peptide and divided by the value of cellular proliferation scored in control cells not in receipt of peptide and wherein cellular proliferation is measured by any suitable means.
16. Use of a peptide sequence specified in Figure 1 or a peptide sequence of at least 9 consecutive amino acid residues of claim 14 or 15 for the manufacture of a byrocin 1 molecule or variants thereof being substantially non-immunogenic or less immunogenic than any non-modified molecule having the same biological activity when used *in vivo*.